Porphyromonas gingivalis as an etiologic factor in the development of neuroinflammation and neurodegeneration - studies on zebrafish model

Popular science summary:

Recent years have brought many evidence that infections and chronic inflammation are at the root of many diseases, including neurodegenerative conditions such as Alzheimer's disease.

The aim of the current project is to investigate whether the bacterium *Porphyromonas gingivalis*, which causes periodontitis, is capable of causing neuroinflammation and, consequently, may cause neurodegeneration.

The research will be carried out on the larvae of a small aquarium fish - zebrafish (*Danio rerio*). This model is often used in biological research, including studies of the immune response to bacterial infections. Using molecular biology methods, a number of zebrafish lines have been created with specifically labeled different types of cells, e.g. leukocytes such as neutrophils and macrophages. Due to the fact that zebrafish larvae are transparent, we can directly observe changes in the morphology of these cells under the microscope, follow their migration and monitor changes in the activity, e.g. the production of radical oxygen species which are toxic to bacteria –. Moreover, zebrafish lines with fluorescently labeled endothelial cells are used to study changes within the blood vessels. Furthermore, the well-known genetics of zebrafish allows to silence expression of the genes of interest, which contributes to our understanding the mechanisms of development of many pathologies.

In the current project, using zebrafish larvae systemically infected with *P. gingivalis*, we will verify whether bacteria enter the brain and cause neuroinflammation, change the brain vessel morphology and activate resident brain immune cells - microglia, and finally lead to the death of neurons. Additionally, we will check whether *P. gingivalis*-induced changes stimulate and/or accelerate the behavioral and neurodegenerative changes characteristic of Alzheimer's disease. We will also investigate whether the administration of molecules inhibiting gingipains, main virulence factors of *P. gingivalis*, can stop the adverse effects of bacteria.

We hope that our research will allow **to determine the mechanism of the neurodegenerative action of *P. gingivalis* and to identify compounds which potentially could support the treatment of patients with this type of pathology** in the near future.